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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,235	RATNER ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 17 August 2007.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-47 is/are pending in the application.

4a) Of the above claim(s) 16-47 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-9, 11-15 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-9, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takei et al. "Dynamic Contact Angle Measurement of Temperature-Responsive Surface Properties for Poly(N-isopropylacrylamide) Grafted Surfaces", Macromolecules 1994, 27, 6163-6166, in view of Carlson et al., 6,939,515.

As to claim 1, Applicants claim a device for binding cells or molecules, wherein the device comprises: a body defining a first surface and a second surface that is located opposite to the first surface; a heater disposed upon the first surface; and a temperature-responsive layer disposed upon the second surface, wherein the temperature-responsive layer comprises a temperature-responsive material that can exist in a first state that binds molecules or living cells, and can exist in a second state that binds substantially less molecules or living cells than the first state, and wherein the temperature-responsive material is reversibly convertible to the first state from the second state in response to an effective amount of thermal energy.

Takei et al. teach that poly(N-isopropylacrylamide) exhibits large swelling changes in aqueous media in response to small changes in temperature and that

temperature-responsive properties of poly(N-isoproplyamide) have been utilized in a variety of applications including controlled drug delivery and solute separation. Takei et al. teach that poly(N-isopropylamide) grated on solid substrates caused temperature-dependent surface properties and that on these surfaces. Poly(N-isopropylacrylamide) on polystyrene dishes were utilized as cell culture substrates and on these surfaces, controlled cell attachment-detachment could be achieved using the reversible hydration-dehydration phenomena of these polymer chains by changing temperature (page 6163, left column.) Thus, Takei et al. teach a temperature-responsive layer, i.e., poly(N-isopropylamide) which can exist in a first state that binds living cells and can exist in a second state that binds less living cells (see disclosure of cell culture and cell-attachment and detachment.)

However while Takei et al. teach an external stimulus that causes a change of temperature which alters the properties of the temperature-responsive material, and specifically disclose that in the experiment, the temperature of circulating water and atmosphere in the measurement chamber was well-controlled (page 1664, right column, under "Dynamic Contact Angle Measurement" heading), Takei et al. do not specifically teach a heater disposed upon a first surface that is located opposite to the surface on which the temperature-responsive material is disposed, as is claimed by Applicants in claim 1.

Carlson et al. however teach an assay device that includes a thermal platform (2810) that can support and controllably heat an array (i.e., a substrate containing samples) (col. 55, lines 6-8, and see fig. 28). Carlson et al. teach that the platform

(2810) includes a thermal platform top (2812) and thermal platform base (2814), which when assembled together create a cavity (2816) that supports a substrate or suitable testing platform (e.g., a carrier plate), (col. 55, lines 11-14). Moreover it is taught by Carlson et al. that in one embodiment the heating elements (2822) may be attached to or embedded in the thermal platform base (2814) to provide a mechanism for heating thermal platform base (2814), (col. 55, lines 64-67). Carlson et al. teach that resistive heating elements (2822) may be embedded or attached to thermal platform base (2814) to permit improved control of thermal control of thermal uniformity or specific temperature profiles in thermal platform (281), and that those skilled in the art will recognize that other methods of heating the thermal platform base (2814) may also be used (col. 56, lines 3-17).

Thus Carlson et al. disclose individually controlled multiple heaters (resistive heating elements). Carlson et al. also teach that the temperature of the thermal platform containing the substrate and material samples can be increased at a defined rate and monitored with one or more temperature sensors that is interfaced with a computer to provide feedback for better temperature control (col. 58, lines 7-15). Moreover, Carlson et al. teach a device with a heater disposed on one surface (i.e., 2814) that is located opposite to the surface on which material samples are located (i.e., the substrate or testing platform disclosed in column 55, lines 13-14), (see figure 28) since the resistive heating elements (2822) is disclosed as being attached to or embedded within thermal platform base (2814) (col. 55, lines 64-67), and the thermal platform base (2814) is part

of thermal platform (2810) which comprises a thermal platform top (2812) and the thermal platform (2814), (col. 55, lines 11-14).

Carlson et al. further teach that for example the temperature of the thermal platform containing the substrate and material samples is increased at a defined rate and monitored with one or more temperature sensors in contact with the substrate and that a computer can be interfaced with the heating system to provide feedback for better temperature control (col. 58, lines 7-15). Carlson et al. disclose that the optical systems allows for simultaneous optical imaging of some or all of the regions on the array (col. 55, lines 6-10). Carlson et al. disclose analyzing an array of samples (col. 32, lines 45-53.)

While Takei et al. teach an external stimulus providing a temperature change but does not disclose the location of the external stimulus with respect to the temperature-responsive material nor any structural details as to this external stimulus, nevertheless it is understood that there is an external stimulus that provides a temperature change. As discussed above, Carlson et al. teach a device equipped with a heating element to heat the substrate containing material sample for an assay. Carlson et al. also teach that the device provides the advantage of improved thermal control of thermal uniformity or specific temperature profiles in thermal platform and that different resistive elements may be capable of distributing different quantities of heat, i.e., the power consumption may vary, and that those skilled in the art will recognize that other methods of heating the thermal platform in a controlled manner may also be used (col. 56, lines 3-17).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a heating element opposite the substrate on which the temperature-responsive material disclosed by Takei et al. is disposed, as taught by Carlson et al., as the specific external stimulus generally disclosed by Takei et al., because Carlson et al. teach that the heating elements in this configuration provides the advantage of improved thermal control of thermal uniformity or specific temperature profiles in thermal platform. Given the disclosures of simultaneous detection of an array of samples, the skilled artisan would recognize the benefits of being able to control the temperature of each assay individually. Moreover Carlson et al. teach that a further advantage of the heating system includes better temperature control through a temperature monitor and a computer for feedback. Thus it would have been obvious to one of ordinary skill in the art to utilize the heating system in the configuration taught by Carlson et al. as the specific external stimulus that is only generally disclosed by Takei et al. particularly in view of the advantages of the heating system taught by Carlson et al. Moreover, while Carlson et al. do not disclose that the heating elements are *on the surface* of a substrate and the assay materials are *on the surface* of the opposite side of the substrate, in the modification of the Takei et al. invention in view of the Carlson et al. teachings, the skilled artisan would need to provide the temperature responsive material on the surface of a substrate, and it is predictable that a heat source whether embedded in the substrate or on the opposite side of the substrate, will provide the temperature control taught by Carlson et al.

As to claim 2, the body consists essentially of glass (see Takei et al., page 6164, bottom of left column.)

As to claims 3 and 5, Takei et al. teach that the glass substrate is 24X50 mm in area and 0.2 mm in thickness (page 6164, bottom of left column), which thus falls within the ranges recited by Applicants.

As to claim 4, Takei et al. teach that the glass slide is 24 mm X 50 mm (which is 12 cm^2)and thus do not specifically teach that the glass slide has an area of 1.0 mm^2 to 5.0 cm^2. However, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. In this case, Takei et al. and Carlson et al. teach the general conditions of the claims (with Takei et al. teaching a substrate with a temperature-responsive material and Carlson et al. teaching a heating element disposed opposite a substrate containing material samples), and thus discovering the workable or optimum range in dimensions of the substrate and heating element involves only routine skill in the art under *In re Aller.*

As to claim 6, Takei et al. teach that the glass substrate is 24X50 mm in area and 0.2 mm in thickness (see Takei et al., page 6164, bottom of left column), which is a rectangular shape of substrate recited by Applicants. As to the shape of the first surface (i.e., heating surface), while Carlson et al. do not disclose the shape of the substrate on which the heating elements are disposed, it would have been an obvious matter of design choice to form the first surface and second surface in rectangular shape, since such a modification would have involved a mere change in the shape of a component

and would also complement the shape of the second surface, i.e., the surface to be heated. A change in shape is generally recognized as being within the level of ordinary skill in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (The court held that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.)

As to claim 7, Applicants claim that the first surface and the second surface are both square. While neither Takei et al. nor Carlson et al. that disclose that the shape of the glass substrate and the substrate on which the heating elements are disposed is square, it would have been an obvious matter of design choice to form the first surface and second surface in square shapes, since such a modification would have involved a mere change in the shape of a component. A change in shape is generally recognized as being within the level of ordinary skill in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966).

As to claims 8 and 9, the temperature-responsive material is poly(N-ethylmethacrylamide) (see Takei et al., page 6163, left column.)

As to claims 11 and 14, a living cell is attached to the temperature-responsive layer (see in Takei et al. reference the disclosure of cell culture and cell-attachment and detachment, page 6163, left column.) As to the location of the living cell opposite the heater, this has been discussed above regarding Carlson et al. (a heater disposed on one surface, 2814, that is located opposite to the surface on which material samples are

located, i.e., the substrate or testing platform disclosed in column 55, lines 13-14, and see figure 28.) The substrate on which the heating elements are disposed, as taught by Carlson et al., is deemed to be the first surface and the substrate on which the temperature-responsive material is disposed is deemed to be the second surface, as claimed by Applicants. Moreover, Carlson et al. teach multiple heaters (2822), (see fig. 28, and col. 55, line 64). The first two heaters (2822) disclosed by Carlson et al. in figure 28 are deemed to form a first population of heaters, and the next two heaters are deemed to form a second population of heaters. As shown by Carlson et al. in figure 28, the heaters are located opposite the testing platform. The portions of temperature-responsive layer that are opposite the first population of heaters is deemed to be the first population of portions, and the portions of temperature-responsive layer that are opposite the second population of heaters is deemed to be the second population of portions.

2. Claims 12, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takei et al. "Dynamic Contact Angle Measurement of Temperature-Responsive Surface Properties for Poly(N-isopropylacrylamide) Grafted Surfaces", Macromolecules 1994, 27, 6163-6166, in view of Carlson et al., 6,939,515, as applied to claim 1 above, and further in view of Lahann et al., 7,020,355

Takei et al. in view of Carlson et al. disclose the invention substantially as claimed (see above).

Takei et al. teach that poly(N-isopropylacrylamide) exhibits large swelling changes in aqueous media in response to small changes in temperature and that temperature-responsive properties of poly(N-isoproplyamide) have been utilized in a variety of applications including controlled drug delivery and solute separation. Takei et al. teach that poly(N-isopropylamide) grated on solid substrates caused temperature-dependent surface properties and that on these surfaces, controlled cell attachment-detachment could be achieved using the reversible hydration-dehydration phenomena of these polymer chains by changing temperature (page 6163, left column.) Takei et al. also teach that end-functionalized poly(N-isopropylacrylamide) will display the largest change in surface properties with change in temperature (page 6163, top of right column.)

While Takei et al. teach controlled cell attachment and detachment on poly(N-isopropylacrylamide) using change in temperature, Takei et al. however do not teach attachment of protein molecules, e.g., antibodies, on the poly(N-isopropylacrylamide).

Lahann et al. teach that self-assembled monolayers have been used to control and pattern the properties of a variety of surfaces and Lahann et al. disclose that it has been found that the wetability of a surface may be controlled by changing the temperature around the lower critical solution temperature of poly(N-isopropylacrylamide)-grafts (col. 1, lines 48-58, citing Takei et al.) Lahann et al. teach that however there is very little research concerning controlled switching between different surface properties (col. 1, lines 49-51). Lahann et al. further state that accordingly it is desirable to develop a method by which the surface properties of a self-

assembled monolayer structure may be reversibly switched upon application or removal of an external force field (col. 1, lines 61-64). Then Lahann et al. teach the disclosed invention comprising a nanolayer that shifts from a first conformation state to a second conformation state upon application of an external stimulus (col. 2, lines 38-40), wherein the external stimulus may be a change in temperature (col. 2, lines 51-53), and Lahann et al. teach reversibly modifying the property of the nanolayer by application of the stimulus to shift the nanolayer from a first absorption affinity to a second absorption affinity, such as an affinity for an analyte (col. 3, lines 40-50).

Thus, Lahann et al. teach that controlling properties of a variety of surfaces are known and Lahann et al. specifically give an example of poly(N-isopropylacrylamide) as a material in which wetability may be controlled by changing temperature. It is noted that Lahann et al. teach that the wetting behavior is defined by the molecular-level structure of the interface (col. 5, lines 5-8, and see lines 30-33). Lahann et al. then teach use of such materials, more specifically, Lahann et al. teach reversibly modifying the properties of such materials by an external stimulus for assay purposes such as concentrating analyte or detecting small quantities of analyte (see col. 24, lines 17-28). Thus, while Lahann et al. do not specifically teach the use of poly(N-isopropylacrylamide) in the disclosed invention, Lahann et al. teach, in general, use of a material that is responsive to temperature (col. 2, lines 51-53), and that a variety of materials that can be controlled are known, including poly(N-isopropylacrylamide), a material in which wetability may be controlled by changing the temperature (col. 1, lines 51-56). However, Lahann et al. specifically teach that the temperature-responsive

material (nanolayer) can be constructed to facilitate adhesion of cells and biomolecules in one conformation and to repel the adhered material or to change the organization of deposited biomolecules in a second conformation (col. 13, line 59 – col. 14, line 3); the term “biomolecules” used by Lahann et al. refers to molecules including proteins and antibodies (col. 4, lines 43-44 and 53.) Lahann et al. further teach that the temperature-responsive nanolayer can be used to facilitate cell attachment for culture, and attachment of analyte and release for detection (col. 24, lines 4-28.)

It is emphasized that Lahann et al. teach that the nanolayer, i.e., a temperature-responsive material, can attach and detach antibodies with a change in conformation and also disclose poly(N-isopropylacrylamide) as a type of temperature-responsive material (citing Takei et al.), and Takei et al. teach that end-functionalized poly(N-isopropylacrylamide) will display the largest change in surface properties with change in temperature (page 6163, top of right column). It appears from the Takei et al. reference that the poly(N-isopropylacrylamide) material can attach and detach materials due to its change in conformation, i.e., surface properties. Takei et al. specifically teach that poly(N-isopropylacrylamide) have been utilized in a variety of applications including controlled drug delivery and solute separation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize poly(N-isopropylacrylamide) taught by Takei et al. to attach antibodies because Lahann et al. teach that temperature-responsive materials provide the benefit of attaching analyte (i.e., biomolecules) and detaching for detection. The skilled artisan would understand the significance of detecting antibodies as

analytes as such biomolecules are detected widely in the art for various diagnostic and medical purposes.

Moreover, the skilled artisan would have reasonable expectation of success in utilizing poly(N-isopropylacrylamide) to attach and detach antibodies since both the teachings of Lahann et al. and Takei et al. teach that a change in surface properties, or conformation, of temperature-responsive material facilitates attachment and detachment of biological materials to the temperature-responsive material, and Takei et al. also teach that poly(N-isopropylacrylamide) has been utilized in a variety of applications including controlled drug delivery and solute separation, which further suggest that poly(N-isopropylamide) can bind to molecules such as antibodies.

As to claim 15, Applicants claim that the multiple heaters comprise a first population of heaters and a second population of heaters, and the temperature-responsive layer comprises a first population of portions, located opposite the first population of heaters, and a second population of portions, located opposite the second population of heaters, wherein a first type of protein molecules is attached to the first population of portions, and a second type of protein molecules is attached to the second population of portions.

The substrate on which the heating elements are disposed, as taught by Carlson et al., is deemed to be the first surface and the substrate on which the temperature-responsive material is disposed is deemed to be the second surface, as claimed by Applicants. Moreover, Carlson et al. teach multiple heaters (2822), (see fig. 28, and col. 55, line 64). The first two heaters (2822) disclosed by Carlson et al. in figure 28 are

deemed to form a first population of heaters, and the next two heaters are deemed to form a second population of heaters. As shown by Carlson et al. in figure 28, the heaters are located opposite the testing platform. The portions of temperature-responsive layer that are opposite the first population of heaters is deemed to be the first population of portions, and the portions of temperature-responsive layer that are opposite the second population of heaters is deemed to be the second population of portions. In the combination of the teachings of Takei et al. and Lahann et al. as discussed above, the protein that is attached to the first population of portions is deemed to be to be a first type of protein, as is claimed by Applicants, and the protein that is attached to the second population of portions is deemed to be a second type of protein (since Applicants do not specify that the first and second type of proteins are different from each other.) (Alternatively, while neither Takei et al. nor Lahann et al. teach different types of proteins in a population of wells or chambers, Carlson teach that this is known in the art to allow for different assays to be performed (col. 25, line 56 – col. 26, line 4), and the skilled artisan would have recognized the benefit of convenience in performing different assays in one substrate as well as the convenience in performing simultaneous assays using different proteins (as regards Applicants' claim 15), or different living cells (as regards Applicants' claim 14.)

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ann Y. Lam
Primary Patent Examiner